REMARKS

In view of the above amendments and the following remarks, the Examiner is respectfully requested to withdraw the rejections and allow Claims 1-20.

Claims 1, 6, 15 and 16 have been amended to specify the duplex nucleic acid molecule is unlabeled. Support for these amendments may be found throughout the specification, e.g., in the experimental section which describes using unlabeled duplex nucleic acids in the practice of the subject invention.

As no new matter has been added by the above amendments, the Applicants respectfully request the entry thereof.

Rejection under 35 U.S.C. §103(a)

Claims 1-16 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Chan (WO 98/35012). The Applicants respectfully submit that Claims 1-16 are patentable over Chan.

As described above, independent Claims 1, 6, 15 and 16, and the claims that depend therefrom, have been amended to specify that the duplex nucleic acid molecule is unlabeled. Accordingly, Chan must teach or suggest a method of characterizing an unlabeled duplex nucleic acid molecule (Claim 1), a method of identifying the presence of an unlabeled duplex nucleic acid (claim 6), or a nanopore device or kit that includes an algorithm for characterizing an unlabeled duplex nucleic acid, in order to render the subject claims unpatentable.

However, Chan does not teach or suggest methods for characterizing an unlabeled duplex nucleic acid based on the identification of a duplex nucleic acid specific signal (Claim 1), or the presence of an unlabeled duplex nucleic acid based on the identification of a duplex nucleic acid specific signal (Claim 6), or a nanopore device or kit that includes an algorithm for characterizing an unlabeled duplex nucleic acid based on evaluating observed current modulations through a nanopore to identify the unlabeled duplex nucleic acid specific signal (Claims 15 and 16) as Chan specifically teaches double stranded DNA that is labeled.

The passages cited by the Examiner in support of this rejection (page 64, lines 29-32 and pages 65-69) specifically refer to nucleic acids that are labeled. For example, the paragraph bridging pages 64-65 teaches:

> "...To reduce the stearic constraints imposed by two extrinsically labeled nucleotides while preserving the theory behind two-nucleotide labeling, it is possible to **label one nucleotide fully on each of the complementary strands to achieve the same end**. This method involves using double-stranded DNA in which **each strand is labeled with a different label...Each complementary strand of DNA should have one of the nucleotides labeled...**" (emphasis added)

Accordingly, Chan does not teach the passage of an unlabeled duplex nucleic acid through a nanopore as Chan specifically teaches labeled double stranded DNA. Furthermore, Chan does not suggest methods for characterizing an unlabeled duplex nucleic acid based on the identification of a duplex nucleic acid specific signal (Claim 1), or the presence of an unlabeled duplex nucleic acid based on the identification of a duplex nucleic acid specific signal (Claim 6), or a nanopore device or kit that includes an algorithm for characterizing an unlabeled duplex nucleic acid based on evaluating observed current modulations through a nanopore to identify the unlabeled duplex nucleic acid specific signal (Claims 15 and 16) as Chan specifically teaches labeled single and double stranded DNA molecules.

Accordingly, for at least the reason that Chan does not teach or suggest an unlabeled duplex nucleic acid molecule as specified in Claims 1, 6, 15 and 16, and the claims that depend therefrom, the Applicants respectfully submit that these claims are patentable over Chan.

In regards to Claims 13 and 14, as noted in the Applicants amendment and response filed August 6, 2003, responsive to the Office Action dated May 6, 2003, these claims are patentable over Chan as Chan fails to teach or suggest all of the claim limitations of these claims.

Claim 13 specifies a method of determining the sequence of a duplex DNA molecule that includes providing a duplex DNA molecule that is protected at one end and blunt ended at the other end and producing a single nucleotide overhang at the blunt end. However, Chan does not teach or suggest a provision of a duplex DNA molecule that is protected at one end and blunt ended at the other end and producing a single nucleotide overhang at the blunt end. Consequently, Chan does not teach or suggest contacting the duplex DNA having a single nucleotide overhang with a nanopore and applying an alternating electric field to the nanopore and monitoring current changes through the nanopore to obtain a set of observed values, also as claimed in Claim 13.

Furthermore, Claim 13 specifies the removal of the single nucleotide overhang from the duplex DNA molecule and repeating the steps of producing a single nucleotide overhang at the blunt end, contacting the duplex DNA having a single nucleotide overhang with a nanopore, applying an alternating electric field to the nanopore, monitoring current changes through the nanopore to obtain a

set of observed values, thus to obtain a collection of observed values for each different duplex nucleic acid produced from the original duplex nucleic acid, and determining the sequence of the duplex DNA molecule from the collection of observed data values. As Chan does not even teach or suggest a provision of a duplex DNA molecule that is protected at one end and blunt ended at the other end and producing a single nucleotide overhang at the blunt end and contacting such a duplex DNA molecule with a nanopore and applying an alternating electric field to the nanopore and monitoring current changes through the nanopore to obtain a set of observed values, Chan does not teach or suggest the removal of the single nucleotide overhang from the duplex DNA molecule and repeating the above-described steps to obtain a collection of observed values for each different duplex nucleic acid produced from the original duplex nucleic acid and determining the sequence of the duplex DNA molecule from the collection of observed data values. Accordingly, Chan does not teach or suggest all the claim limitations of Claim 13.

Accordingly, for at least the reasons described above, Chan does not teach or suggest all of the claim limitations of Claims 1-16. As such, the Applicants respectfully submit that these claims are patentable over Chan.

As the Examiner did not specifically address the Applicants' arguments with respect to Claims 13 and 14, the Applicants respectfully request the Examiner to point to the teachings of Chan that refer to the subject matter specified in Claims 13 and 14, or provide reasoning why the Examiner believes it would be obvious to modify the teachings of Chan to provide such, in the next communication if the rejection of Claims 13 and 14 is maintained. Specifically, the Applicants respectfully request the Examiner to point to the teachings of Chan that the Examiner believes refer to the provision of a duplex DNA molecule that is protected at one end and blunt ended at the other end, the production of a single nucleotide overhang at the blunt end, and the removal of the single nucleotide overhang from the duplex DNA molecule, and repeating the steps of producing a single nucleotide overhang at the blunt end, contacting the duplex DNA having a single nucleotide overhang with a nanopore, applying an alternating electric field to the nanopore, monitoring current changes through the nanopore to obtain a set of observed values, thus to obtain a collection of observed values for each different duplex nucleic acid produced from the original duplex nucleic acid, and the determination of the sequence of the duplex DNA molecule from the collection of observed data values.

Accordingly, for at least the reasons described above, the Applicants respectfully request the rejection of Claims 1-16 over Chan be withdrawn.

Allowance

The Applicants thank the Examiner for the indication of allowance of Claims 17-20.

CONCLUSION

In view of the above amendments and remarks, this application is considered to be in good and proper form for allowance and the Examiner is respectfully requested to pass this application to issuance. The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, Order No. UCAL199.

Respectfully submitted,
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